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WP+ 136P1 CRP-001-CP3 01/03/90

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Rueger et al.	Examiner:	N. Nutter
Serial No.:	422,699	Group Art Unit:	153
Filed:	October 17, 1989	Attorney Docket:	CRP-001-CP3
Title:	OSTEOGENIC PROTEIN		

Honorable Commissioner of Patents and Trademarks
Washington, DC 20231

****
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Honorable Commissioner of Patents and Trademarks, Washington, D.C. 20231 on the date set forth below.

Jan 17, 1990 By Edmund R Pitcher
Date of Signature and of Mail Deposit
Edmund R. Pitcher
Registration No. 27,829
Attorney for Applicant

****

LETTER TO THE OFFICIAL DRAFTSMAN

Dear Sir:

Enclosed is a copy of the Notice of Patent Drawing Objection in the above-referenced application, and new drawings, correcting the informalities.

Respectfully submitted,

LAHIVE & COCKFIELD

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Reg. No. 27,829

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Date: 1/17/90

PTO - 948
(Rev. 8-82)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

ATTACHMENT TO PAPER NUMBER 2

GROUP 153

S.N. 422699

NOTICE OF PATENT DRAWINGS OBJECTION

Drawing Corrections and/or new drawings may only be submitted in the manner set forth in the attached letter, "Information on How to Effect Drawing Changes" PTO-1474.

A. ☒ The drawings, filed on 10-17-89, are objected to as informal for reason(s) checked below:

1. ☐ Lines Pale.
2. ☐ Paper Poor.
3. ☐ Numerals Poor.
4. ☐ Lines Rough and Blurred.
5. ☐ Shade Lines Required.
6. ☐ Figures Must be Numbered.
7. ☒ Heading Space Required. 1" top. Fig. 1A-1
8. ☐ Figures Must Not be Connected.
9. ☐ Criss-Cross Hatching Objectionable.
10. ☐ Double-Line Hatching Objectionable.
11. ☐ Parts in Section Must Be Hatched.
12. ☐ Solid Black Objectionable.
13. ☐ Figure Legends Placed Incorrectly.
14. ☐ Mounted Photographs.
15. ☐ Extraneous Matter Objectionable. [37 CFR 1.84 (1)]
16. ☐ Paper Undersized; either 8½" x 14", or 21.0 cm. x 29.7 cm. required.
17. ☐ Proper A4 Margins Required:
    ☐ TOP 2.5 cm. ☐ RIGHT 1.5 cm.
    ☐ LEFT 2.5 cm. ☐ BOTTOM 1.0 cm.
18. ☒ Other:
    - Fig. legends small must be Fig (1A-1)-(3-2) bigger

B. ☒ The drawings, submitted on 10-17-89, are so informal they cannot be corrected. New drawings are required. Submission of the new drawings MUST be made in accordance with the attached letter.

Cancel

07/422699

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GGAGGTATAGGAGCTCTCTTCGATTTTAGCAAACCAGGAGTCCGAAGATCTAAGGAGAGC
TGGGGGTTTGACTCCGAGAGCTCGAGCAGTCCCCAAGACCTGGTCTTGACTCACGAGTTA
GACTCCACTCAGAGGCTGACTGTCTCCAGGGTCTACACCTCTAAGGGCGACACTGGGCTC
AAGCAGACTGCCGTTTTCTATATGGGATGAGCCTTCACAGGGCAGCCAGTTGGGATGGGT
TGAGGTTTGGCTGTAGACATCAGAAACCCAAGTCAAATGCGCTTCAACCAGTAGAAAATT
CACCAGCCCGCAGAGCTAAGGTTGGGTGGACATTAGGGTTGGTTGATCCAGGAGCTCAAC
AGTGTCCTCTGAGCCCCAGCTCCTTCTGCCCCACCCCACCATCTTCAGTGCTGCTTCCTC
TCAAGGCCACAGCTGTAGTTGGCCAGGGGGGCTTCATTATTTTTTGCTCCTGGGCAGTAG
GAGGAAGAGAATGAATGTCTCTCCATGGGTCTTTCTTAGGAATGTGGGAACTTTTTCCAG
AAGTCTCTATGTCTTTTAGTTTGTGTTGGGTCACTTGCCCTTCCTGAACCACTTCCTGAC
TCCTGGACAGGATGTGCACTGATGAGCTTAGCTTTGGGGATCTAATAGTGACTTTACAAA
GCCTCTTTGAGAAGGTGACATTGGAACCAAGGCTTGAGCAGACACAACAAAGATTGCAGG
GAGGGGCATTGCAGGTGGAGGAAACGGCACATGCAAGAGCCCTGCGTGGGAGTGAGCTTG
GTGTTTGGTCAATCAGTTGTCAGAGCACACCGGGCCCTGTCAGCAGGCACAGCCTGGGCC
TGCTCTGAGTATGACAGAGAGCCCCTGGGAAGTTGTAGGTGGAGGAAAGACAGGTCATGA
CTAGGAAAAAAGCAATCCCTCTGTTGTGGGGTGGAAGGAAGGTTGCAGTGTGTGTGAGAG
AGAGACAAGACAGACAGACAGACACTTCTCAATGTTTACAAGTGCTCAGGCCCTGACCCG
AATGCTTCCAAATTTACGTAGTTCTGGAAAACCCCCTGTATCATTTTCACTACTCAAAGA
AACCTCGGGAGTGTTTTCTTCTGAAAGGTCATCAGGTTTTGACTCTCTGCTGTCTCATTT
CTTCTTGCTGGTGGTGGTGATGGTTGCTTGTCCCAGGCCCTGTCCCGCATCCTCTTGCCC
CTGCAGAGGGATGAGTGTGTTGGGGCCTCACGAGTTGAGGTTGTTCATAAGCAGATCTCT
TTGAGCAGGGCGCCTGCAGTGGCCTTGTGTGAGGCTGGAGGGGTTTCGATTCCCTTATGG
AATCCAGGCAGATGTAGCATTTAAACAACACACGTGTATAAAAGAAACCAGTGTCCGCAG
AAGGTTCCAGAAAGTATTATGGGATAAGACTACATGAGAGAGGAATGGGGCATTGGCACC
TCCCTTAGTAGGGCCTTTGCTGGGGGTAGAAATGAGTTTTAAGGCAGGTTAGACCCTCGA
ACTGGCTTTTGAATCGGGAAATTTACCCCCCAGCCGTTCTGTGCTTCATTGCTGTTCACA
TCACTGCCTAAGATGGAGGAACTTTGATGTGTGTGTGTTTCTTTCTCCTCACTGGGCTCT
GCTTCTTCACTTCCTTGTCAAT
;intron=exon
                          GCAGAGAACAGCAGCAGCGACCAGAGGCAGGCCTGTA
                           A  E  N  S  S  S  D  Q  R  Q  A  C
AGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAG
K  K  H  E  L  Y  V  S  F  R  D  L  G  W  Q

;exon=intron
                                                    GTAAGGGGCTGGCTGG
GTCTGTCTTGGGTGTGGGCCCTCTGGCGTGGGCTCCCACAGGCAGCGGGTGCTGTGCTCA
GTCTTGTTTCTCATCTCTGCCAGTTAAGACTCCAGTATCAAGTGGCCTCGCTAGGGAAGG
GTACTTGGCTAAGGATACAGGG.....................................
.GGGAGCCAGCATGGGTGATGCCATTATGAGTTATTAGCCTCTCTGGCAGGTGGGCAAAC
CGAGGCATGGAGGTTTGTTTAAGGTGAACTGCCAGTGTGTGACCACCTAGTGGGGTAGAG
CTGATGATTGCCTCACACCGGAGCTCCTTCCTGTGCCGCGTTCTGTCCAGAAGACACAGC
CATGGATGTCCATTTTAGGATCAGCCAAGCCCCGTCTTGTCCTTCATTTTTATTTTATGT
TTTTTTAGAAATGGGGTCTTGCTCTGTCACCCAGGCTGGGTGCAGTGGTGTGATCATAGC
TCACCGCAGCTTTGACGCCGTCTTCCCACTCAGTCTACTAAGCTTGGACTATAGGCCAAG
ACTATAGAGTGGTCCTTCTTTCCATTCTTTTGGGACCATGAGAGGCCACCCATGTTTCCT
GCCCCTGCTGGGCCCTGCTGCTCAGAAGGCATGGTCTGAGGCTTTCACCTTGGTCGTGAG
CCTTCGTGGTGGTTTCTTTCAGCATGGGGTTGGGATGCTGTGCTCAGGCTTCTGCATGGT
TTCCCACACTCTCTTCTCCTCCTCAG
;intron=exon
```

FIG. 1A-1

```
                                GACTGGATCATCGCGCCTGAAGGCTACGCCGCCT
                                 D  W  I  I  A  P  E  G  Y  A  A
ACTACTGTGAGGGGGAGTGTGCCTTCCCTCTGAACTCCTACATGAACGCCACCAACCACG
Y  Y  C  E  G  E  C  A  F  P  L  N  S  Y  M  N  A  T  N  H
CCATCGTGCAGACGCTG
A  I  V  Q  T  L
;exon=intron

                                GTGGGTGTCACGCCATCTTGGGGTGTGGTCACCTGGGCCGGGC
AGGCTGCGGGGCCACCAGATCCTGCTGCCTCCAAGCTGGGGCCTGAGTAGATGTCAGCCC
ATTGCCATGTCATGACTTTTGGGGGCCCCTTGCGCCGTTAAAAAAAAATCAAAAATTGTA
CTTTATGACTGGTTTGGTATAAAGAGGAGTATAATCTTCGACCCTGGAGTTCATTTATTT
CTCCTAATTTTTAAAGTAACTAAAAGTTGTATGGGCTCCTTTGAGGATGCTTGTAGTATT
GTGGGTGCTGGTTACGGTGCCTAAGAGCACTGGGCCCCTGCTTCATTTTCCAGTAGAGGA
AACAGGTAAACAGATGAGAAATTTCAGTGAGGGGCACAGTGATCAGAAGCGGGCCAGCAG
GATAATGGGATGGAGAGATGAGTGGGGACCCATGGGCCATTTCAAGTTAAATTTCAGTCG
GGTCACCAGGAAGATTCCATGTGATAATGAGATTAACGTGCCCAGTCACGGCGACACTCA
GTAGGTGTTATTCCTGCTCTGCCAACAGCAACCATAGTTGATAAGAGCTGTTAGGGATTT
TGTCCTTTTGCTTAGAATCCAAGGTTCAAGGACCTTGGTTATGTAGCTCCCTGTCATGAA
CATCATCTGAGCCTTTCCTGCCTACTGATCATCCACCCTGCCTTGAATGCTTCTAGTGAC
AGAGAGCTCACTACCAGGACTACTCCCTCCTTTCATTTAGTAATCTGCCTCCTTCTTTTC
TTGTCCCTGTCCTGTGTGTTAAGTCCTGGAGAAAAATCTCATCTATCCCTTTCATTTGAT
TCTGCTCTTTGAGGGCAGGGGTTTTTGTTTCTTTGTTTGTTTTTTTAAGTGTTGGTTTTC
CAAAGCCCTTGCTCCCCTCCTCAATTGAAACTTCAAAGCCCTCATTGGGATTGAAGGTCC
TTAGGCTGGAAACAGAAGAGTCCTCCCCAACCTGTTCCCTGGCCTGGATGTGCTGTGCTG
TGCCAGTATCCCCTGGAAGGTGCCAGGCATGTCTCCCCGGCTGCCAGGGGACACATCTCT
ATCCTTCTCCAACCCCTGCCTTCATGGCCCATGGAACAGGAGTGCCATCGCCCTGTGTGC
ACCTACTTCCATCAGTATTTCACCAGAGATCTGCAGGATCAAAGTGAATTCTCCAGGGAT
TGTGAAATGATGCGATTGTGGTCATGTTTAAAAGGGGGCAACTGTCTTCTAGAGAGTCCT
GATGAAATGCTTCCAGAGGAAATGAGCTGATGGCTGGAATTTGCTTTAAAATCATTCAAG
GTGGAGCAGGTGGGGAAGGGTATGGATGTGTAAGAGTTTGAAATTGTCCATCATAAAATG
TGTAAAAAGCATGCTGGCCTATGTCAGCAGTCACAGCCTGGAGGTGGTAACAGAGTGCCA
GTCACTGATGCTCAAGCCTGGCACCTACAGTTGCTGGAAACCCAGAAGTTTCACGTTGAA
AACAACAGGACAGTGGAATCTCTGGCCCTGTCTTGAACACGTGGCAGATCTGCTAACACT
GATCTTGGTTGGCTGCCGTCAGCTTAGGTTGAGTGGCGGTCTTCCCTTAGTTTGCTTAGT
CCCCGCTATTCCCTATTGTCTTACCTCGGTCTATTTTGCTTATCAGTGGACCTCACGAGG
CACTCATAGGCATTTGAGTCTATGTGTCCCTGTCCCACATCCTCTGTAAGGTGCAGAGAA
GTCCATGAGCAAGATGGAGCACTTCTAGTGGGTCCAAGTCAGGGACACTATTCAGCAATC
TACAGTGCACAGGGCAGTTCCCCAACAGAGAATTACCTGGTCCTGAATGTCGGATCTGGC
CCCTTCCTTCCCCACTGTATAATGTGAAAACCTCTATGCTTTGTTCCCCTTGTCTGCAAA
ACAGGGATAATCCCAGAACTGAGTTGTCCATGTAAAGTGCTTAGAACAGGGAGTGCTTGG
CTTGGGGAGTGTCACCTGCAGTCATTCATTATGCCCAGACAGGATGTTTCTTTATAGAAA
CGTGGAGGCCAGTTAGAACGACTCACCGCTTCTCACCACTGCCCATGTTTTGGTGTGTGT
TTCAG
;intron=exon
   GTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCCACGCAGC
    V  H  F  I  N  P  E  T  V  P  K  P  C  C  A  P  T  Q
TCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACA
L  N  A  I  S  V  L  Y  F  D  D  S  S  N  V  I  L  K  K  Y
GAAACATGGTGGTCCGGGCCTGTGGCTGCCACTAGCTCCTCCGAGAATTC
R  N  M  V  V  R  A  C  G  C  H
```

FIG. 1A-2

```
        10         20         30         40         50         60
GGTGCGGGCCCGGAGCCCGGAGCCCGGGTAGCGCGTAGAGCCGGCGCGATGCACGTGCGC
                                                   M  H  V  R
        70         80         90        100        110        120
TCACTGCGAGCTGCGGCGCCGCACAGCTTCGTGGCGCTCTGGGCACCCCTGTTCCTGCTG
 S  L  R  A  A  A  P  H  S  F  V  A  L  W  A  P  L  F  L  L
       130        140        150        160        170        180
CGCTCCGCCCTGGCCGACTTCAGCCTGGACAACGAGGTGCACTCGAGCTTCATCCACCGG
 R  S  A  L  A  D  F  S  L  D  N  E  V  H  S  S  F  I  H  R
    -  -  -  -  -
       190        200        210        220        230        240
CGCCTCCGCAGCCAGGAGCGGCGGGAGATGCAGCGCGAGATCCTCTCCATTTTGGGCTTG
 R  L  R  S  Q  E  R  R  E  M  Q  R  E  I  L  S  I  L  G  L
       250        260        270        280        290        300
CCCCACCGCCCGCGCCCGCACCTCCAGGGCAAGCACAACTCGGCACCCATGTTCATGCTG
 P  H  R  P  R  P  H  L  Q  G  K  H  N  S  A  P  M  F  M  L
       310        320        330        340        350        360
GACCTGTACAACGCCATGGCGGTGGAGGAGGGCGGCGGGCCCGGCGGCCAGGGCTTCTCC
 D  L  Y  N  A  M  A  V  E  E  G  G  G  P  G  G  Q  G  F  S
       370        380        390        400        410        420
TACCCCTACAAGGCCGTCTTCAGTACCCAGGGCCCCCCTCTGGCCAGCCTGCAAGATAGC
 Y  P  Y  K  A  V  F  S  T  Q  G  P  P  L  A  S  L  Q  D  S
       430        440        450        460        470        480
CATTTCCTCACCGACGCCGACATGGTCATGAGCTTCGTCAACCTCGTGGAACATGACAAG
 H  F  L  T  D  A  D  M  V  M  S  F  V  N  L  V  E  H  D  K
       490        500        510        520        530        540
GAATTCTTCCACCCACGCTACCACCATCGAGAGTTCCGGTTTGATCTTTCCAAGATCCCA
 E  F  F  H  P  R  Y  H  H  R  E  F  R  F  D  L  S  K  I  P
       550        560        570        580        590        600
GAAGGGGAAGCTGTCACGGCAGCCGAATTCCGGATCTACAAGGACTACATCCGGGAACGC
 E  G  E  A  V  T  A  A  E  F  R  I  Y  K  D  Y  I  R  E  R
       610        620        630        640        650        660
TTCGACAATGAGACGTTCCGGATCAGCGTTTATCAGGTGCTCCAGGAGCACTTGGGCAGG
 F  D  N  E  T  F  R  I  S  V  Y  Q  V  L  Q  E  H  L  G  R
       670        680        690        700        710        720
GAATCGGATCTCTTCCTGCTCGACAGCCGTACCCTCTGGGCCTCGGAGGAGGGCTGGCTG
 E  S  D  L  F  L  L  D  S  R  T  L  W  A  S  E  E  G  W  L
       730        740        750        760        770        780
GTGTTTGACATCACAGCCACCAGCAACCACTGGGTGGTCAATCCGCGGCACAACCTGGGC
 V  F  D  I  T  A  T  S  N  H  W  V  V  N  P  R  H  N  L  G
       790        800        810        820        830        840
CTGCAGCTCTCGGTGGAGACGCTGGATGGGCAGAGCATCAACCCCAAGTTGGCGGGCCTG
 L  Q  L  S  V  E  T  L  D  G  Q  S  I  N  P  K  L  A  G  L
       850        860        870        880        890        900
ATTGGGCGGCACGGGCCCCAGAACAAGCAGCCCTTCATGGTGGCTTTCTTCAAGGCCACG
 I  G  R  H  G  P  Q  N  K  Q  P  F  M  V  A  F  F  K  A  T
       910        920        930        940        950        960
GAGGTCCACTTCCGCAGCATCCGGTCCACGGGGAGCAAACAGCGCAGCCAGAACCGCTCC
 E  V  H  F  R  S  I  R  S  T  G  S  K  Q  R  S  Q  N  R  S
                                      *  *  *  *  *  *  *  *
       970        980        990       1000       1010       1020
AAGACGCCCAAGAACCAGGAAGCCCTGCGGATGGCCAACGTGGCAGAGAACAGCAGCAGC
 K  T  P  K  N  Q  E  A  L  R  M  A  N  V  A  E  N  S  S  S
 *  *  *  *
```

FIG. 1B-1 OP1 CDNA

```
     1030       1040       1050       1060       1070       1080
GACCAGAGGCAGGCCTGTAAGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGG
 D  Q  R  Q  A  C  K  K  H  E  L  Y  V  S  F  R  D  L  G  W
      1090       1100       1110       1120       1130       1140
CAGGACTGGATCATCGCGCCTGAAGGCTACGCCGCCTACTACTGTGAGGGGGAGTGTGCC
 Q  D  W  I  I  A  P  E  G  Y  A  A  Y  Y  C  E  G  E  C  A
      1150       1160       1170       1180       1190       1200
TTCCCTCTGAACTCCTACATGAACGCCACCAACCACGCCATCGTGCAGACGCTGGTCCAC
 F  P  L  N  S  Y  M  N  A  T  N  H  A  I  V  Q  T  L  V  H
      1210       1220       1230       1240       1250       1260
TTCATCAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCCACGCAGCTCAATGCCATC
 F  I  N  P  E  T  V  P  K  P  C  C  A  P  T  Q  L  N  A  I
      1270       1280       1290       1300       1310       1320
TCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACAGAAACATGGTG
 S  V  L  Y  F  D  D  S  S  N  V  I  L  K  K  Y  R  N  M  V
      1330       1340       1350       1360       1370       1380
GTCCGGGCCTGTGGCTGCCACTAGCTCCTCCGAGAATTCAGACCCTTTGGGGCCAAGTTT
 V  R  A  C  G  C  H  *
      1390       1400       1410       1420       1430       1440
TTCTGGATCCTCCATTGCTCGCCTTGGCCAGGAACCAGCAGACCAACTGCCTTTTGTGAG
      1450       1460       1470       1480       1490       1500
ACCTTCCCCTCCCTATCCCCAACTTTAAAGGTGTGAGAGTATTAGGAAACATGAGCAGCA
      1510       1520       1530       1540       1550       1560
TATGGCTTTTGATCAGTTTTTCAGTGGCAGCATCCAATGAACAAGATCCTACAAGCTGTG
      1570       1580       1590       1600       1610       1620
CAGGCAAAACCTAGCAGGAAAAAAAAACAACGCATAAAGAAAAATGGCCGGGCCAGGTCA
      1630       1640       1650       1660       1670       1680
TTGGCTGGGAAGTCTCAGCCATGCACGGACTCGTTTCCAGAGGTAATTATGAGCGCCTAC
      1690       1700       1710       1720       1730       1740
CAGCCAGGCCACCCAGCCGTGGGAGGAAGGGGGCGTGGCAAGGGGTGGGCACATTGGTGT
      1750       1760       1770       1780       1790       1800
CTGTGCGAAAGGAAAATTGACCCGGAAGTTCCTGTAATAAATGTCACAATAAAACGAATG
      1810       1820
AATGAAAAAAAAAAAAAAAAAA
```

FIG. 1B-2 OP1 CDNA

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CONSENSUS PROBE   20        30        40        50        60        70
GATCCTAATGGGCTGTACGTGGACTTCCAGCGCGACGTGGGCTGGGACGACTGGATCATCGCCCCCGTCG
      **                        ** *** ********   ************** **
TGTAAGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGGACTGGATCATCGCGCCTGAAG
OP1      28        38        48        58        68        78        88

         80        90       100       110       120       130       140
ACTTCGACGCCTACTACTGCTCCGGAGCCTGCCAGTTCCCCTCTGCGGATCACTTCAACAGCACCAACCA
 ** **    *********    **    **    *****           **   ***  *********
GCTACGCGCGCTACTACTGTGAGGGGGAGTGTGCCTTCCCTCTGAACTCCTACATGAACGCCACCAACCA
         98       108       118       128       138       148       158

        150       160       170       180       190       200       210
CGCCGTGGTGCAGACCCTGGTGAACAACATGAACCCCGGCAAGGTACCCAAGCCCTGCTGCGTGCCCACC
****   ******** *****  **  *** *****      *** **************   ******
CGCCATCGTGCAGACGCTGGTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCCACG
        168       178       188       198       208       218       228

        220       230       240       250       260       270       280
GAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATTCCACCGTGGTGCTGAAGAACTACCAGGAGA
 ****    ******      ** ***   ** **    **** ***    ******** ***      *
CAGCTCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACAGAAACA
        238       248       258       268       278       288       298

        290       300       310
TGACCGTGGTGGGCTGCGGCTGCCGCTAACTGCA
**   **   ** *** ******* *** **
TGGTGGTCCGGGCCTGTGGCTGCCACTAGCTCCT
        308       318       328
```

FIGURE 1C

```
        10         20         30         40         50         60
TCGACTCTAGAGTGTGTGTCAGCACTTGGCTGGGGACTTCTTGAACTTGCAGGGAGAATA
        70         80         90        100        110        120
ACTTGCGCACCCCACTTTGCGCCGGTGCCTTTGCCCCAGCGGAGCCTGCTTCGCCATCTC
       130        140        150        160        170        180
CGAGCCCCACCGCCCCTCCACTCCTCGGCCTTGCCCGACACTGAGACGCTGTTCCCAGCG
       190        200        210        220        230        240
TGAAAAGAGAGACTGCGCGGCCGGCACCCGGGAGAAGGAGGAGGCAAAGAAAAGGAACGG
       250        260        270        280        290        300
ACATTCGGTCCTTGCGCCAGGTCCTTTGACCAGAGTTTTTCCATGTGGACGCTCTTTCAA
       310        320        330        340        350        360
TGGACGTGTCCCCGCGTGCTTCTTAGACGGACTGCGGTCTCCTAAAGGTCGACCATGGTG
                                                          M  V
       370        380        390        400        410        420
GCCGGGACCCGCTGTCTTCTAGCGTTGCTGCTTCCCCAGGTCCTCCTGGGCGGCGCGGCT
 A  G  T  R  C  L  L  A  L  L  L  P  Q  V  L  L  G  G  A  A
       430        440        450        460        470        480
GGCCTCGTTCCGGAGCTGGGCCGCAGGAAGTTCGCGGCGGCGTCGTCGGGCCGCCCCTCA
 G  L  V  P  E  L  G  R  R  K  F  A  A  A  S  S  G  R  P  S
       490        500        510        520        530        540
TCCCAGCCCTCTGACGAGGTCCTGAGCGAGTTCGAGTTGCGGCTGCTCAGCATGTTCGGC
 S  Q  P  S  D  E  V  L  S  E  F  E  L  R  L  L  S  M  F  G
       550        560        570        580        590        600
CTGAAACAGAGACCCACCCCCAGCAGGGACGCCGTGGTGCCCCCCTACATGCTAGACCTG
 L  K  Q  R  P  T  P  S  R  D  A  V  V  P  P  Y  M  L  D  L
       610        620        630        640        650        660
TATCGCAGGCACTCGGGTCAGCCGGGCTCACCCGCCCCAGACCACCGGTTGGAGAGGGCA
 Y  R  R  H  S  G  Q  P  G  S  P  A  P  D  H  R  L  E  R  A
       670        680        690        700        710        720
GCCAGCCGAGCCAACACTGTGCGCAGCTTCCACCATGAAGAATCTTTGGAAGAACTACCA
 A  S  R  A  N  T  V  R  S  F  H  H  E  E  S  L  E  E  L  P
       730        740        750        760        770        780
GAAACGAGTGGGAAAACAACCCGGAGATTCTTCTTTAATTTAAGTTCTATCCCCACGGAG
 E  T  S  G  K  T  T  R  R  F  F  F  N  L  S  S  I  P  T  E
       790        800        810        820        830        840
GAGTTTATCACCTCAGCAGAGCTTCAGGTTTTCCGAGAACAGATGCAAGATGCTTTAGGA
 E  F  I  T  S  A  E  L  Q  V  F  R  E  Q  M  Q  D  A  L  G
       850        860        870        880        890        900
AACAATAGCAGTTTCCATCACCGAATTAATATTTATGAAATCATAAAACCTGCAACAGCC
 N  N  S  S  F  H  H  R  I  N  I  Y  E  I  I  K  P  A  T  A
       910        920        930        940        950        960
AACTCGAAATTCCCCGTGACCAGTCTTTTGGACACCAGGTTGGTGAATCAGAATGCAAGC
 N  S  K  F  P  V  T  S  L  L  D  T  R  L  V  N  Q  N  A  S
       970        980        990       1000       1010       1020
AGGTGGGAAAGTTTTGATGTCACCCCCGCTGTGATGCGGTGGACTGCACAGGGACACGCC
 R  W  E  S  F  D  V  T  P  A  V  M  R  W  T  A  Q  G  H  A
      1030       1040       1050       1060       1070       1080
AACCATGGATTCGTGGTGGAAGTGGCCCACTTGGAGGAGAAACAAGGTGTCTCCAAGAGA
 N  H  G  F  V  V  E  V  A  H  L  E  E  K  Q  G  V  S  K  R
```

FIG. 2-1

```
      1090       1100       1110       1120       1130       1140
CATGTTAGGATAAGCAGGTCTTTGCACCAAGATGAACACAGCTGGTCACAGATAAGGCCA
 H  V  R  I  S  R  S  L  H  Q  D  E  H  S  W  S  Q  I  R  P
      1150       1160       1170       1180       1190       1200
TTGCTAGTAACTTTTGGCCATGATGGAAAAGGGCATCCTCTCCACAAAAGAGAAAAACGT
 L  L  V  T  F  G  H  D  G  K  G  H  P  L  H  K  R  E::K  R
      1210       1220       1230       1240       1250       1260
CAAGCCAAACACAAACAGCGGAAACGCCTTAAGTCCAGCTGTAAGAGACACCCTTTGTAC
 Q  A  K  H  K  Q  R  K  R  L  K  S  S  C  K  R  H  P  L  Y
      1270       1280       1290       1300       1310       1320
GTGGACTTCAGTGACGTGGGGTGGAATGACTGGATTGTGGCTCCCCCGGGGTATCACGCC
 V  D  F  S  D  V  G  W  N  D  W  I  V  A  P  P  G  Y  H  A
      1330       1340       1350       1360       1370       1380
TTTTACTGCCACGGAGAATGCCCTTTTCCTCTGGCTGATCATCTGAACTCCACTAATCAT
 F  Y  C  H  G  E  C  P  F  P  L  A  D  H  L  N  S  T  N  H
      1390       1400       1410       1420       1430       1440
GCCATTGTTCAGACGTTGGTCAACTCTGTTAACTCTAAGATTCCTAAGGCATGCTGTGTC
 A  I  V  Q  T  L  V  N  S  V  N  S  K  I  P  K  A  C  C  V
      1450       1460       1470       1480       1490       1500
CCGACAGAACTCAGTGCTATCTCGATGCTGTACCTTGACGAGAATGAAAAGGTTGTATTA
 P  T  E  L  S  A  I  S  M  L  Y  L  D  E  N  E  K  V  V  L
      1510       1520       1530       1540       1550       1560
AAGAACTATCAGGACATGGTTGTGGAGGGTTGTGGGTGTCGCTAGTACAGCAAAATTAAA
 K  N  Y  Q  D  M  V  V  E  G  C  G  C  R  *
      1570       1580       1590
TACATAAATATATATATATATATATATTTTAGAAAAAAGAAAAAAA
```

FIG. 2-2

```
        10         20         30         40         50         60
CTCTAGAGGGCAGAGGAGGAGGGAGGGAGGGAAGGAGCGCGGAGCCCGGCCCGGAAGCTA
        70         80         90        100        110        120
GGTGAGTGTGGCATCCGAGCTGAGGGACGCGAGCCTGAGACGCCGCTGCTGCTCCGGCTG
       130        140        150        160        170        180
AGTATCTAGCTTGTCTCCCCGATGGGATTCCCGTCCAAGCTATCTCGAGCCTGCAGCGCC
       190        200        210        220        230        240
ACAGTCCCCGGCCCTCGCCCAGGTTCACTGCAACCGTTCAGAGGTCCCCAGGAGCTGCTG
       250        260        270        280        290        300
CTGGCGAGCCCGCTACTGCAGGGACCTATGGAGCCATTCCGTAGTGCCATCCCGAGCAAC
       310        320        330        340        350        360
GCACTGCTGCAGCTTCCCTGAGCCTTTCCAGCAAGTTTGTTCAAGATTGGCTGTCAAGAA
       370        380        390        400        410        420
TCATGGACTGTTATTATATGCCTTGTTTTCTGTCAAGACACCATGATTCCTGGTAACCGA
                                                  M  I  P  G  N  R
       430        440        450        460        470        480
ATGCTGATGGTCGTTTTATTATGCCAAGTCCTGCTAGGAGGCGCGAGCCATGCTAGTTTG
 M  L  M  V  V  L  L  C  Q  V  L  L  G  G  A  S  H  A  S  L
       490        500        510        520        530        540
ATACCTGAGACGGGGAAGAAAAAAGTCGCCGAGATTCAGGGCCACGCGGGAGGACGCCGC
 I  P  E  T  G  K  K  K  V  A  E  I  Q  G  H  A  G  G  R  R
       550        560        570        580        590        600
TCAGGGCAGAGCCATGAGCTCCTGCGGGACTTCGAGGCGACACTTCTGCAGATGTTTGGG
 S  G  Q  S  H  E  L  L  R  D  F  E  A  T  L  L  Q  M  F  G
       610        620        630        640        650        660
CTGCGCCGCCGCCCGCAGCCTAGCAAGAGTGCCGTCATTCCGGACTACATGCGGGATCTT
 L  R  R  R  P  Q  P  S  K  S  A  V  I  P  D  Y  M  R  D  L
       670        680        690        700        710        720
TACCGGCTTCAGTCTGGGGAGGAGGAGGAAGAGCAGATCCACAGCACTGGTCTTGAGTAT
 Y  R  L  Q  S  G  E  E  E  E  E  Q  I  H  S  T  G  L  E  Y
       730        740        750        760        770        780
CCTGAGCGCCCGGCCAGCCGGGCCAACACCGTGAGGAGCTTCCACCACGAAGAACATCTG
 P  E  R  P  A  S  R  A  N  T  V  R  S  F  H  H  E  E  H  L
       790        800        810        820        830        840
GAGAACATCCCAGGGACCAGTGAAAACTCTGCTTTTCGTTTCCTCTTTAACCTCAGCAGC
 E  N  I  P  G  T  S  E  N  S  A  F  R  F  L  F  N  L  S  S
       850        860        870        880        890        900
ATCCCTGAGAACGAGGTGATCTCCTCTGCAGAGCTTCGGCTCTTCCGGGAGCAGGTGGAC
 I  P  E  N  E  V  I  S  S  A  E  L  R  L  F  R  E  Q  V  D
       910        920        930        940        950        960
CAGGGCCCTGATTGGGAAAGGGGCTTCCACCGTATAAACATTTATGAGGTTATGAAGCCC
 Q  G  P  D  W  E  R  G  F  H  R  I  N  I  Y  E  V  M  K  P
       970        980        990       1000       1010       1020
CCAGCAGAAGTGGTGCCTGGGCACCTCATCACACGACTACTGGACACGAGACTGGTCCAC
 P  A  E  V  V  P  G  H  L  I  T  R  L  L  D  T  R  L  V  H
      1030       1040       1050       1060       1070       1080
CACAATGTGACACGGTGGGAAACTTTTGATGTGAGCCCTGCGGTCCTTCGCTGGACCCGG
 H  N  V  T  R  W  E  T  F  D  V  S  P  A  V  L  R  W  T  R
      1090       1100       1110       1120       1130       1140
GAGAAGCAGCCAAACTATGGGCTAGCCATTGAGGTGACTCACCTCCATCAGACTCGGACC
 E  K  Q  P  N  Y  G  L  A  I  E  V  T  H  L  H  Q  T  R  T
```

FIG. 3-1

```
      1150       1160       1170       1180       1190       1200
CACCAGGGCCAGCATGTCAGGATTAGCCGATCGTTACCTCAAGGGAGTGGGAATTGGGCC
 H  Q  G  Q  H  V  R  I  S  R  S  L  P  Q  G  S  G  N  W  A
      1210       1220       1230       1240       1250       1260
CAGCTCCGGCCCCTCCTGGTCACCTTTGGCCATGATGGCCGGGGCCATGCCTTGACCCGA
 Q  L  R  P  L  L  V  T  F  G  H  D  G  R  G  H  A  L  T  R
      1270       1280       1290       1300       1310       1320
CGCCGGAGGGCCAAGCGTAGCCCTAAGCATCACTCACAGCGGGCCAGGAAGAAGAATAAG
 R  R  R  A::K  R  S  P  K  H  H  S  Q  R  A  R  K  K  N  K
      1330       1340       1350       1360       1370       1380
AACTGCCGGCGCCACTCGCTCTATGTGGACTTCAGCGATGTGGGCTGGAATGACTGGATT
 N  C  R  R  H  S  L  Y  V  D  F  S  D  V  G  W  N  D  W  I
      1390       1400       1410       1420       1430       1440
GTGGCCCCACCAGGCTACCAGGCCTTCTACTGCCATGGGGACTGCCCCTTTCCACTGGCT
 V  A  P  P  G  Y  Q  A  F  Y  C  H  G  D  C  P  F  P  L  A
      1450       1460       1470       1480       1490       1500
GACCACCTCAACTCAACCAACCATGCCATTGTGCAGACCCTGGTCAATTCTGTCAATTCC
 D  H  L  N  S  T  N  H  A  I  V  Q  T  L  V  N  S  V  N  S
      1510       1520       1530       1540       1550       1560
AGTATCCCCAAAGCCTGTTGTGTGCCCACTGAACTGAGTGCCATCTCCATGCTGTACCTG
 S  I  P  K  A  C  C  V  P  T  E  L  S  A  I  S  M  L  Y  L
      1570       1580       1590       1600       1610       1620
GATGAGTATGATAAGGTGGTACTGAAAAATTATCAGGAGATGGTAGTAGAGGGATGTGGG
 D  E  Y  D  K  V  V  L  K  N  Y  Q  E  M  V  V  E  G  C  G
      1630       1640       1650       1660       1670       1680
TGCCGCTGAGATCAGGCAGTCCTTGAGGATAGACAGATATACACACACACACACACACAC
 C  R  *
      1690       1700       1710       1720       1730       1740
CACATACACCACACACACACGTTCCCATCCACTCACCCACACACTACACAGACTGCTTCC
      1750       1760       1770       1780       1790       1800
TTATAGATGGACTTTTATTTAAAAAAAAAAAAAAAAAAAATGGAAAAAATCCCTAAACATT
      1810       1820       1830       1840       1850       1860
CACCTTGACCTTATTTATGACTTTACGTGCAAATGTTTTGACCATATTGATCATATATTT
      1870       1880       1890       1900       1910       1920
TGACAAAATATATTTATAACTACGTATTAAAAGAAAAAAATAAAATGAGTCATTATTTTA
      1930
AAAAAAAAAAAAAAA
```

FIG. 3-2

```
GGAGGTATAGGAGCTCTCTTCGATTTTAGCAAACCAGGAGTCCGAAGATCTAAGGAGAGC
TGGGGGTTTGACTCCGAGAGCTCGAGCAGTCCCCAAGACCTGGTCTTGACTCACGAGTTA
GACTCCACTCAGAGGCTGACTGTCTCCAGGGTCTACACCTCTAAGGGCGACACTGGGCTC
AAGCAGACTGCCGTTTTCTATATGGGATGAGCCTTCACAGGGCAGCCAGTTGGGATGGGT
TGAGGTTTGGCTGTAGACATCAGAAACCCAAGTCAAATGCGCTTCAACCAGTAGAAAATT
CACCAGCCCGCAGAGCTAAGGTTGGGTGGACATTAGGGTTGGTTGATCCAGGAGCTCAAC
AGTGTCCTCTGAGCCCCAGCTCCTTCTGCCCCACCCCACCATCTTCAGTGCTGCTTCCTC
TCAAGGCCACAGCTGTAGTTGGCCAGGGGGGCTTCATTATTTTTTGCTCCTGGGCAGTAG
GAGGAAGAGAATGAATGTCTCTCCATGGGTCTTTCTTAGGAATGTGGGAACTTTTTCCAG
AAGTCTCTATGTCTTTTAGTTTGTGTTGGGTCACTTGCCCTTCCTGAACCACTTCCTGAC
TCCTGGACAGGATGTGCACTGATGAGCTTAGCTTTGGGGATCTAATAGTGACTTTACAAA
GCCTCTTTGAGAAGGTGACATTGGAACCAAGGCTTGAGCAGACACAACAAAGATTGCAGG
GAGGGGCATTGCAGGTGGAGGAAACGGCACATGCAAGAGCCCTGCGTGGGAGTGAGCTTG
GTGTTTGGTCAATCAGTTGTCAGAGCACACCGGGCCCTGTCAGCAGGCACAGCCTGGGCC
TGCTCTGAGTATGACAGAGAGCCCCTGGGAAGTTGTAGGTGGAGGAAAGACAGGTCATGA
CTAGGAAAAAAGCAATCCCTCTGTTGTGGGGTGGAAGGAAGGTTGCAGTGTGTGTGAGAG
AGAGACAAGACAGACAGACAGACACTTCTCAATGTTTACAAGTGCTCAGGCCCTGACCCG
AATGCTTCCAAATTTACGTAGTTCTGGAAAACCCCCTGTATCATTTTCACTACTCAAAGA
AACCTCGGGAGTGTTTTCTTCTGAAAGGTCATCAGGTTTTGACTCTCTGCTGTCTCATTT
CTTCTTGCTGGTGGTGGTGATGGTTGCTTGTCCCAGGCCCTGTCCCGCATCCTCTTGCCC
CTGCAGAGGGATGAGTGTGTTGGGGCCTCACGAGTTGAGGTTGTTCATAAGCAGATCTCT
TTGAGCAGGGCGCCTGCAGTGGCCTTGTGTGAGGCTGGAGGGGTTTCGATTCCCTTATGG
AATCCAGGCAGATGTAGCATTTAAACAACACACGTGTATAAAAGAAACCAGTGTCCGCAG
AAGGTTCCAGAAAGTATTATGGGATAAGACTACATGAGAGAGGAATGGGGCATTGGCACC
TCCCTTAGTAGGGCCTTTGCTGGGGGTAGAAATGAGTTTTAAGGCAGGTTAGACCCTCGA
ACTGGCTTTTGAATCGGGAAATTTACCCCCCAGCCGTTCTGTGCTTCATTGCTGTTCACA
TCACTGCCTAAGATGGAGGAACTTTGATGTGTGTGTGTTTCTTTCTCCTCACTGGGCTCT
GCTTCTTCACTTCCTTGTCAAT
;intron=exon
                                GCAGAGAACAGCAGCAGCGACCAGAGGCAGGCCTGTA
                                 A  E  N  S  S  S  D  Q  R  Q  A  C
AGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAG
K  K  H  E  L  Y  V  S  F  R  D  L  G  W  Q

;exon=intron

                                                        GTAAGGGGCTGGCTGG
GTCTGTCTTGGGTGTGGGCCCTCTGGCGTGGGCTCCCACAGGCAGCGGGTGCTGTGCTCA
GTCTTGTTTCTCATCTCTGCCAGTTAAGACTCCAGTATCAAGTGGCCTCGCTAGGGAAGG
GTACTTGGCTAAGGATACAGGG.....................................
.GGGAGCCAGCATGGGTGATGCCATTATGAGTTATTAGCCTCTCTGGCAGGTGGGCAAAC
CGAGGCATGGAGGTTTGTTTAAGGTGAACTGCCAGTGTGTGACCACCTAGTGGGGTAGAG
CTGATGATTGCCTCACACCGGAGCTCCTTCCTGTGCCGCGTTCTGTCCAGAAGACACAGC
CATGGATGTCCATTTTAGGATCAGCCAAGCCCCGTCTTGTCCTTCATTTTTATTTTATGT
TTTTTTAGAAATGGGGTCTTGCTCTGTCACCCAGGCTGGGTGCAGTGGTGTGATCATAGC
TCACCGCAGCTTTGACGCCGTCTTCCCACTCAGTCTACTAAGCTTGGACTATAGGCCAAG
ACTATAGAGTGGTCCTTCTTTCCATTCTTTTGGGACCATGAGAGGCCACCCATGTTTCCT
GCCCCTGCTGGGCCCTGCTGCTCAGAAGGCATGGTCTGAGGCTTTCACCTTGGTCGTGAG
CCTTCGTGGTGGTTTCTTTCAGCATGGGGTTGGGATGCTGTGCTCAGGCTTCTGCATGGT
TTCCCACACTCTCTTCTCCTCCTCAG
;intron=exon
```

FIG. 1A-1

```
                          GACTGGATCATCGCGCCTGAAGGCTACGCCGCCT
                            D  W  I  I  A  P  E  G  Y  A  A
ACTACTGTGAGGGGGAGTGTGCCTTCCCTCTGAACTCCTACATGAACGCCACCAACCACG
Y  Y  C  E  G  E  C  A  F  P  L  N  S  Y  M  N  A  T  N  H
CCATCGTGCAGACGCTG
A  I  V  Q  T  L
;exon=intron

                      GTGGGTGTCACGCCATCTTGGGGTGTGGTCACCTGGGCCGGGC
AGGCTGCGGGGCCACCAGATCCTGCTGCCTCCAAGCTGGGGCCTGAGTAGATGTCAGCCC
ATTGCCATGTCATGACTTTTGGGGGCCCCTTGCGCCGTTAAAAAAAAATCAAAAATTGTA
CTTTATGACTGGTTTGGTATAAAGAGGAGTATAATCTTCGACCCTGGAGTTCATTTATTT
CTCCTAATTTTTAAAGTAACTAAAAGTTGTATGGGCTCCTTTGAGGATGCTTGTAGTATT
GTGGGTGCTGGTTACGGTGCCTAAGAGCACTGGGCCCCTGCTTCATTTTCCAGTAGAGGA
AACAGGTAAACAGATGAGAAATTTCAGTGAGGGGCACAGTGATCAGAAGCGGGCCAGCAG
GATAATGGGATGGAGAGATGAGTGGGGACCCATGGGCCATTTCAAGTTAAATTTCAGTCG
GGTCACCAGGAAGATTCCATGTGATAATGAGATTAACGTGCCCAGTCACGGCGACACTCA
GTAGGTGTTATTCCTGCTCTGCCAACAGCAACCATAGTTGATAAGAGCTGTTAGGGATTT
TGTCCTTTTGCTTAGAATCCAAGGTTCAAGGACCTTGGTTATGTAGCTCCCTGTCATGAA
CATCATCTGAGCCTTTCCTGCCTACTGATCATCCACCCTGCCTTGAATGCTTCTAGTGAC
AGAGAGCTCACTACCAGGACTACTCCCTCCTTTCATTTAGTAATCTGCCTCCTTCTTTTC
TTGTCCCTGTCCTGTGTGTTAAGTCCTGGAGAAAAATCTCATCTATCCCTTTCATTTGAT
TCTGCTCTTTGAGGGCAGGGGTTTTTGTTTCTTTGTTTGTTTTTTTAAGTGTTGGTTTTC
CAAAGCCCTTGCTCCCCTCCTCAATTGAAACTTCAAAGCCCTCATTGGGATTGAAGGTCC
TTAGGCTGGAAACAGAAGAGTCCTCCCCAACCTGTTCCCTGGCCTGGATGTGCTGTGCTG
TGCCAGTATCCCCTGGAAGGTGCCAGGCATGTCTCCCCGGCTGCCAGGGGACACATCTCT
ATCCTTCTCCAACCCCTGCCTTCATGGCCCATGGAACAGGAGTGCCATCGCCCTGTGTGC
ACCTACTTCCATCAGTATTTCACCAGAGATCTGCAGGATCAAAGTGAATTCTCCAGGGAT
TGTGAAATGATGCGATTGTGGTCATGTTTAAAAGGGGGCAACTGTCTTCTAGAGAGTCCT
GATGAAATGCTTCCAGAGGAAATGAGCTGATGGCTGGAATTTGCTTTAAAATCATTCAAG
GTGGAGCAGGTGGGGAAGGGTATGGATGTGTAAGAGTTTGAAATTGTCCATCATAAAATG
TGTAAAAAGCATGCTGGCCTATGTCAGCAGTCACAGCCTGGAGGTGGTAACAGAGTGCCA
GTCACTGATGCTCAAGCCTGGCACCTACAGTTGCTGGAAACCCAGAAGTTTCACGTTGAA
AACAACAGGACAGTGGAATCTCTGGCCCTGTCTTGAACACGTGGCAGATCTGCTAACACT
GATCTTGGTTGGCTGCCGTCAGCTTAGGTTGAGTGGCGGTCTTCCCTTAGTTTGCTTAGT
CCCCGCTATTCCCTATTGTCTTACCTCGGTCTATTTTGCTTATCAGTGGACCTCACGAGG
CACTCATAGGCATTTGAGTCTATGTGTCCCTGTCCCACATCCTCTGTAAGGTGCAGAGAA
GTCCATGAGCAAGATGGAGCACTTCTAGTGGGTCCAAGTCAGGGACACTATTCAGCAATC
TACAGTGCACAGGGCAGTTCCCCAACAGAGAATTACCTGGTCCTGAATGTCGGATCTGGC
CCCTTCCTTCCCCACTGTATAATGTGAAAACCTCTATGCTTTGTTCCCCTTGTCTGCAAA
ACAGGGATAATCCCAGAACTGAGTTGTCCATGTAAAGTGCTTAGAACAGGGAGTGCTTGG
CTTGGGGAGTGTCACCTGCAGTCATTCATTATGCCCAGACAGGATGTTTCTTTATAGAAA
CGTGGAGGCCAGTTAGAACGACTCACCGCTTCTCACCACTGCCCATGTTTTGGTGTGTGT
TTCAG
;intron=exon
   GTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCCACGCAGC
     V  H  F  I  N  P  E  T  V  P  K  P  C  C  A  P  T  Q
TCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACA
L  N  A  I  S  V  L  Y  F  D  D  S  S  N  V  I  L  K  K  Y
GAAACATGGTGGTCCGGGCCTGTGGCTGCCACTAGCTCCTCCGAGAATTC
R  N  M  V  V  R  A  C  G  C  H
```

FIG. 1A-2

```
        10         20         30         40         50         60
GGTGCGGGCCCGGAGCCCGGAGCCCGGGTAGCGCGTAGAGCCGGCGCGATGCACGTGCGC
                                                  M  H  V  R
        70         80         90        100        110        120
TCACTGCGAGCTGCGGCGCCGCACAGCTTCGTGGCGCTCTGGGCACCCCTGTTCCTGCTG
 S  L  R  A  A  A  P  H  S  F  V  A  L  W  A  P  L  F  L  L
       130        140        150        160        170        180
CGCTCCGCCCTGGCCGACTTCAGCCTGGACAACGAGGTGCACTCGAGCTTCATCCACCGG
 R  S  A  L  A  D  F  S  L  D  N  E  V  H  S  S  F  I  H  R
    -  -  -  -  -
       190        200        210        220        230        240
CGCCTCCGCAGCCAGGAGCGGCGGGAGATGCAGCGCGAGATCCTCTCCATTTTGGGCTTG
 R  L  R  S  Q  E  R  R  E  M  Q  R  E  I  L  S  I  L  G  L
       250        260        270        280        290        300
CCCCACCGCCCGCGCCCGCACCTCCAGGGCAAGCACAACTCGGCACCCATGTTCATGCTG
 P  H  R  P  R  P  H  L  Q  G  K  H  N  S  A  P  M  F  M  L
       310        320        330        340        350        360
GACCTGTACAACGCCATGGCGGTGGAGGAGGGCGGCGGGCCCGGCGGCCAGGGCTTCTCC
 D  L  Y  N  A  M  A  V  E  E  G  G  G  P  G  G  Q  G  F  S
       370        380        390        400        410        420
TACCCCTACAAGGCCGTCTTCAGTACCCAGGGCCCCCCTCTGGCCAGCCTGCAAGATAGC
 Y  P  Y  K  A  V  F  S  T  Q  G  P  P  L  A  S  L  Q  D  S
       430        440        450        460        470        480
CATTTCCTCACCGACGCCGACATGGTCATGAGCTTCGTCAACCTCGTGGAACATGACAAG
 H  F  L  T  D  A  D  M  V  M  S  F  V  N  L  V  E  H  D  K
       490        500        510        520        530        540
GAATTCTTCCACCCACGCTACCACCATCGAGAGTTCCGGTTTGATCTTTCCAAGATCCCA
 E  F  F  H  P  R  Y  H  H  R  E  F  R  F  D  L  S  K  I  P
       550        560        570        580        590        600
GAAGGGGAAGCTGTCACGGCAGCCGAATTCCGGATCTACAAGGACTACATCCGGGAACGC
 E  G  E  A  V  T  A  A  E  F  R  I  Y  K  D  Y  I  R  E  R
       610        620        630        640        650        660
TTCGACAATGAGACGTTCCGGATCAGCGTTTATCAGGTGCTCCAGGAGCACTTGGGCAGG
 F  D  N  E  T  F  R  I  S  V  Y  Q  V  L  Q  E  H  L  G  R
       670        680        690        700        710        720
GAATCGGATCTCTTCCTGCTCGACAGCCGTACCCTCTGGGCCTCGGAGGAGGGCTGGCTG
 E  S  D  L  F  L  L  D  S  R  T  L  W  A  S  E  E  G  W  L
       730        740        750        760        770        780
GTGTTTGACATCACAGCCACCAGCAACCACTGGGTGGTCAATCCGCGGCACAACCTGGGC
 V  F  D  I  T  A  T  S  N  H  W  V  V  N  P  R  H  N  L  G
       790        800        810        820        830        840
CTGCAGCTCTCGGTGGAGACGCTGGATGGGCAGAGCATCAACCCCAAGTTGGCGGGCCTG
 L  Q  L  S  V  E  T  L  D  G  Q  S  I  N  P  K  L  A  G  L
       850        860        870        880        890        900
ATTGGGCGGCACGGGCCCCAGAACAAGCAGCCCTTCATGGTGGCTTTCTTCAAGGCCACG
 I  G  R  H  G  P  Q  N  K  Q  P  F  M  V  A  F  F  K  A  T
       910        920        930        940        950        960
GAGGTCCACTTCCGCAGCATCCGGTCCACGGGGAGCAAACAGCGCAGCCAGAACCGCTCC
 E  V  H  F  R  S  I  R  S  T  G  S  K  Q  R  S  Q  N  R  S
                                    *  *  *  *  *  *  *  *
       970        980        990       1000       1010       1020
AAGACGCCCAAGAACCAGGAAGCCCTGCGGATGGCCAACGTGGCAGAGAACAGCAGCAGC
 K  T  P  K  N  Q  E  A  L  R  M  A  N  V  A  E  N  S  S  S
 *  *  *  *
```

FIG. 1B-1 OP1 CDNA

```
     1030       1040       1050       1060       1070       1080
GACCAGAGGCAGGCCTGTAAGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGG
 D  Q  R  Q  A  C  K  K  H  E  L  Y  V  S  F  R  D  L  G  W
     1090       1100       1110       1120       1130       1140
CAGGACTGGATCATCGCGCCTGAAGGCTACGCCGCCTACTACTGTGAGGGGGAGTGTGCC
 Q  D  W  I  I  A  P  E  G  Y  A  A  Y  Y  C  E  G  E  C  A
     1150       1160       1170       1180       1190       1200
TTCCCTCTGAACTCCTACATGAACGCCACCAACCACGCCATCGTGCAGACGCTGGTCCAC
 F  P  L  N  S  Y  M  N  A  T  N  H  A  I  V  Q  T  L  V  H
     1210       1220       1230       1240       1250       1260
TTCATCAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCCACGCAGCTCAATGCCATC
 F  I  N  P  E  T  V  P  K  P  C  C  A  P  T  Q  L  N  A  I
     1270       1280       1290       1300       1310       1320
TCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACAGAAACATGGTG
 S  V  L  Y  F  D  D  S  S  N  V  I  L  K  K  Y  R  N  M  V
     1330       1340       1350       1360       1370       1380
GTCCGGGCCTGTGGCTGCCACTAGCTCCTCCGAGAATTCAGACCCTTTGGGGCCAAGTTT
 V  R  A  C  G  C  H  *
     1390       1400       1410       1420       1430       1440
TTCTGGATCCTCCATTGCTCGCCTTGGCCAGGAACCAGCAGACCAACTGCCTTTTGTGAG
     1450       1460       1470       1480       1490       1500
ACCTTCCCCTCCCTATCCCCAACTTTAAAGGTGTGAGAGTATTAGGAAACATGAGCAGCA
     1510       1520       1530       1540       1550       1560
TATGGCTTTTGATCAGTTTTTCAGTGGCAGCATCCAATGAACAAGATCCTACAAGCTGTG
     1570       1580       1590       1600       1610       1620
CAGGCAAAAACCTAGCAGGAAAAAAAAAACAACGCATAAAGAAAAATGGCCGGGCCAGGTCA
     1630       1640       1650       1660       1670       1680
TTGGCTGGGAAGTCTCAGCCATGCACGGACTCGTTTCCAGAGGTAATTATGAGCGCCTAC
     1690       1700       1710       1720       1730       1740
CAGCCAGGCCACCCAGCCGTGGGAGGAAGGGGGCGTGGCAAGGGGTGGGCACATTGGTGT
     1750       1760       1770       1780       1790       1800
CTGTGCGAAAGGAAAATTGACCCGGAAGTTCCTGTAATAAATGTCACAATAAAACGAATG
     1810       1820
AATGAAAAAAAAAAAAAAAAAA
```

FIG. 1B-2 OP1 CDNA

```
CONSENSUS PROBE   20         30         40         50         60         70
GATCCTAATGGGCTGTACGTGGACTTCCAGCGCGACGTGGGCTGGGACGACTGGATCATCGCCCCCGTCG
      **                        ** *** ********   ***************  **
TGTAAGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGGACTGGATCATCGCGCCTGAAG
OP1     28         38         48         58         68         78         88

        80         90        100        110        120        130        140
ACTTCGACGCCTACTACTGCTCCGGAGCCTGCCAGTTCCCCTCTGCGGATCACTTCAACAGCACCAACCA
 **  **    *********     **    **  .  *****              **   ***  *********
GCTACGCGCGCTACTACTGTGAGGGGGAGTGTGCCTTCCCTCTGAACTCCTACATGAACGCCACCAACCA
        98        108        118        128        138        148        158

       150        160        170        180        190        200        210
CGCCGTGGTGCAGACCCTGGTGAACAACATGAACCCCGGCAAGGTACCCAAGCCCTGCTGCGTGCCCACC
****   ******** *****  **  *** *****       *** **************   ******
CGCCATCGTGCAGACGCTGGTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCCACG
       168        178        188        198        208        218        228

       220        230        240        250        260        270        280
GAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATTCCACCGTGGTGCTGAAGAACTACCAGGAGA
 ****    ******        ** ***   ** **    **** ***    ********* ***       *
CAGCTCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACAGAAACA
       238        248        258        268        278        288        298

       290        300        310
TGACCGTGGTGGGCTGCGGCTGCCGCTAACTGCA
**   **    ** *** ******* *** **
TGGTGGTCCGGGCCTGTGGCTGCCACTAGCTCCT
       308        318        328
```

FIGURE 1C

```
        10         20         30         40         50         60
TCGACTCTAGAGTGTGTGTCAGCACTTGGCTGGGGACTTCTTGAACTTGCAGGGAGAATA
        70         80         90        100        110        120
ACTTGCGCACCCCACTTTGCGCCGGTGCCTTTGCCCCAGCGGAGCCTGCTTCGCCATCTC
       130        140        150        160        170        180
CGAGCCCCACCGCCCCTCCACTCCTCGGCCTTGCCCGACACTGAGACGCTGTTCCCAGCG
       190        200        210        220        230        240
TGAAAAGAGAGACTGCGCGGCCGGCACCCGGGAGAAGGAGGAGGCAAAGAAAAGGAACGG
       250        260        270        280        290        300
ACATTCGGTCCTTGCGCCAGGTCCTTTGACCAGAGTTTTTCCATGTGGACGCTCTTTCAA
       310        320        330        340        350        360
TGGACGTGTCCCCGCGTGCTTCTTAGACGGACTGCGGTCTCCTAAAGGTCGACCATGGTG
                                                          M  V
       370        380        390        400        410        420
GCCGGGACCCGCTGTCTTCTAGCGTTGCTGCTTCCCCAGGTCCTCCTGGGCGGCGCGGCT
 A  G  T  R  C  L  L  A  L  L  L  P  Q  V  L  L  G  G  A  A
       430        440        450        460        470        480
GGCCTCGTTCCGGAGCTGGGCCGCAGGAAGTTCGCGGCGGCGTCGTCGGGCCGCCCCTCA
 G  L  V  P  E  L  G  R  R  K  F  A  A  A  S  S  G  R  P  S
       490        500        510        520        530        540
TCCCAGCCCTCTGACGAGGTCCTGAGCGAGTTCGAGTTGCGGCTGCTCAGCATGTTCGGC
 S  Q  P  S  D  E  V  L  S  E  F  E  L  R  L  L  S  M  F  G
       550        560        570        580        590        600
CTGAAACAGAGACCCACCCCCAGCAGGGACGCCGTGGTGCCCCCCTACATGCTAGACCTG
 L  K  Q  R  P  T  P  S  R  D  A  V  V  P  P  Y  M  L  D  L
       610        620        630        640        650        660
TATCGCAGGCACTCGGGTCAGCCGGGCTCACCCGCCCCAGACCACCGGTTGGAGAGGGCA
 Y  R  R  H  S  G  Q  P  G  S  P  A  P  D  H  R  L  E  R  A
       670        680        690        700        710        720
GCCAGCCGAGCCAACACTGTGCGCAGCTTCCACCATGAAGAATCTTTGGAAGAACTACCA
 A  S  R  A  N  T  V  R  S  F  H  H  E  E  S  L  E  E  L  P
       730        740        750        760        770        780
GAAACGAGTGGGAAAACAACCCGGAGATTCTTCTTTAATTTAAGTTCTATCCCCACGGAG
 E  T  S  G  K  T  T  R  R  F  F  F  N  L  S  S  I  P  T  E
       790        800        810        820        830        840
GAGTTTATCACCTCAGCAGAGCTTCAGGTTTTCCGAGAACAGATGCAAGATGCTTTAGGA
 E  F  I  T  S  A  E  L  Q  V  F  R  E  Q  M  Q  D  A  L  G
       850        860        870        880        890        900
AACAATAGCAGTTTCCATCACCGAATTAATATTTATGAAATCATAAAACCTGCAACAGCC
 N  N  S  S  F  H  H  R  I  N  I  Y  E  I  I  K  P  A  T  A
       910        920        930        940        950        960
AACTCGAAATTCCCCGTGACCAGTCTTTTGGACACCAGGTTGGTGAATCAGAATGCAAGC
 N  S  K  F  P  V  T  S  L  L  D  T  R  L  V  N  Q  N  A  S
       970        980        990       1000       1010       1020
AGGTGGGAAAGTTTTGATGTCACCCCCGCTGTGATGCGGTGGACTGCACAGGGACACGCC
 R  W  E  S  F  D  V  T  P  A  V  M  R  W  T  A  Q  G  H  A
      1030       1040       1050       1060       1070       1080
AACCATGGATTCGTGGTGGAAGTGGCCCACTTGGAGGAGAAACAAGGTGTCTCCAAGAGA
 N  H  G  F  V  V  E  V  A  H  L  E  E  K  Q  G  V  S  K  R
```

FIG. 2-1

```
      1090       1100       1110       1120       1130       1140
CATGTTAGGATAAGCAGGTCTTTGCACCAAGATGAACACAGCTGGTCACAGATAAGGCCA
 H  V  R  I  S  R  S  L  H  Q  D  E  H  S  W  S  Q  I  R  P
      1150       1160       1170       1180       1190       1200
TTGCTAGTAACTTTTGGCCATGATGGAAAAGGGCATCCTCTCCACAAAAGAGAAAAACGT
 L  L  V  T  F  G  H  D  G  K  G  H  P  L  H  K  R  E::K  R
      1210       1220       1230       1240       1250       1260
CAAGCCAAACACAAACAGCGGAAACGCCTTAAGTCCAGCTGTAAGAGACACCCTTTGTAC
 Q  A  K  H  K  Q  R  K  R  L  K  S  S  C  K  R  H  P  L  Y
      1270       1280       1290       1300       1310       1320
GTGGACTTCAGTGACGTGGGGTGGAATGACTGGATTGTGGCTCCCCCGGGGTATCACGCC
 V  D  F  S  D  V  G  W  N  D  W  I  V  A  P  P  G  Y  H  A
      1330       1340       1350       1360       1370       1380
TTTTACTGCCACGGAGAATGCCCTTTTCCTCTGGCTGATCATCTGAACTCCACTAATCAT
 F  Y  C  H  G  E  C  P  F  P  L  A  D  H  L  N  S  T  N  H
      1390       1400       1410       1420       1430       1440
GCCATTGTTCAGACGTTGGTCAACTCTGTTAACTCTAAGATTCCTAAGGCATGCTGTGTC
 A  I  V  Q  T  L  V  N  S  V  N  S  K  I  P  K  A  C  C  V
      1450       1460       1470       1480       1490       1500
CCGACAGAACTCAGTGCTATCTCGATGCTGTACCTTGACGAGAATGAAAAGGTTGTATTA
 P  T  E  L  S  A  I  S  M  L  Y  L  D  E  N  E  K  V  V  L
      1510       1520       1530       1540       1550       1560
AAGAACTATCAGGACATGGTTGTGGAGGGTTGTGGGTGTCGCTAGTACAGCAAAATTAAA
 K  N  Y  Q  D  M  V  V  E  G  C  G  C  R  *
      1570       1580       1590
TACATAAATATATATATATATATATATTTTAGAAAAAAGAAAAAAA
```

FIG. 2-2

```
        10         20         30         40         50         60
CTCTAGAGGGCAGAGGAGGAGGGAGGGAGGGAAGGAGCGCGGAGCCCGGCCCGGAAGCTA
        70         80         90        100        110        120
GGTGAGTGTGGCATCCGAGCTGAGGGACGCGAGCCTGAGACGCCGCTGCTGCTCCGGCTG
       130        140        150        160        170        180
AGTATCTAGCTTGTCTCCCCGATGGGATTCCCGTCCAAGCTATCTCGAGCCTGCAGCGCC
       190        200        210        220        230        240
ACAGTCCCCGGCCCTCGCCCAGGTTCACTGCAACCGTTCAGAGGTCCCCAGGAGCTGCTG
       250        260        270        280        290        300
CTGGCGAGCCCGCTACTGCAGGGACCTATGGAGCCATTCCGTAGTGCCATCCCGAGCAAC
       310        320        330        340        350        360
GCACTGCTGCAGCTTCCCTGAGCCTTTCCAGCAAGTTTGTTCAAGATTGGCTGTCAAGAA
       370        380        390        400        410        420
TCATGGACTGTTATTATATGCCTTGTTTTCTGTCAAGACACCATGATTCCTGGTAACCGA
                                                  M  I  P  G  N  R
       430        440        450        460        470        480
ATGCTGATGGTCGTTTTATTATGCCAAGTCCTGCTAGGAGGCGCGAGCCATGCTAGTTTG
 M  L  M  V  V  L  L  C  Q  V  L  L  G  G  A  S  H  A  S  L
       490        500        510        520        530        540
ATACCTGAGACGGGGAAGAAAAAAGTCGCCGAGATTCAGGGCCACGCGGGAGGACGCCGC
 I  P  E  T  G  K  K  K  V  A  E  I  Q  G  H  A  G  G  R  R
       550        560        570        580        590        600
TCAGGGCAGAGCCATGAGCTCCTGCGGGACTTCGAGGCGACACTTCTGCAGATGTTTGGG
 S  G  Q  S  H  E  L  L  R  D  F  E  A  T  L  L  Q  M  F  G
       610        620        630        640        650        660
CTGCGCCGCCGCCCGCAGCCTAGCAAGAGTGCCGTCATTCCGGACTACATGCGGGATCTT
 L  R  R  R  P  Q  P  S  K  S  A  V  I  P  D  Y  M  R  D  L
       670        680        690        700        710        720
TACCGGCTTCAGTCTGGGGAGGAGGAGGAAGAGCAGATCCACAGCACTGGTCTTGAGTAT
 Y  R  L  Q  S  G  E  E  E  E  E  Q  I  H  S  T  G  L  E  Y
       730        740        750        760        770        780
CCTGAGCGCCCGGCCAGCCGGGCCAACACCGTGAGGAGCTTCCACCACGAAGAACATCTG
 P  E  R  P  A  S  R  A  N  T  V  R  S  F  H  H  E  E  H  L
       790        800        810        820        830        840
GAGAACATCCCAGGGACCAGTGAAAACTCTGCTTTTCGTTTCCTCTTTAACCTCAGCAGC
 E  N  I  P  G  T  S  E  N  S  A  F  R  F  L  F  N  L  S  S
       850        860        870        880        890        900
ATCCCTGAGAACGAGGTGATCTCCTCTGCAGAGCTTCGGCTCTTCCGGGAGCAGGTGGAC
 I  P  E  N  E  V  I  S  S  A  E  L  R  L  F  R  E  Q  V  D
       910        920        930        940        950        960
CAGGGCCCTGATTGGGAAAGGGGCTTCCACCGTATAAACATTTATGAGGTTATGAAGCCC
 Q  G  P  D  W  E  R  G  F  H  R  I  N  I  Y  E  V  M  K  P
       970        980        990       1000       1010       1020
CCAGCAGAAGTGGTGCCTGGGCACCTCATCACACGACTACTGGACACGAGACTGGTCCAC
 P  A  E  V  V  P  G  H  L  I  T  R  L  L  D  T  R  L  V  H
      1030       1040       1050       1060       1070       1080
CACAATGTGACACGGTGGGAAACTTTTGATGTGAGCCCTGCGGTCCTTCGCTGGACCCGG
 H  N  V  T  R  W  E  T  F  D  V  S  P  A  V  L  R  W  T  R
      1090       1100       1110       1120       1130       1140
GAGAAGCAGCCAAACTATGGGCTAGCCATTGAGGTGACTCACCTCCATCAGACTCGGACC
 E  K  Q  P  N  Y  G  L  A  I  E  V  T  H  L  H  Q  T  R  T
```

FIG. 3-1

```
     1150       1160       1170       1180       1190       1200
CACCAGGGCCAGCATGTCAGGATTAGCCGATCGTTACCTCAAGGGAGTGGGAATTGGGCC
 H  Q  G  Q  H  V  R  I  S  R  S  L  P  Q  G  S  G  N  W  A
     1210       1220       1230       1240       1250       1260
CAGCTCCGGCCCCTCCTGGTCACCTTTGGCCATGATGGCCGGGGCCATGCCTTGACCCGA
 Q  L  R  P  L  L  V  T  F  G  H  D  G  R  G  H  A  L  T  R
     1270       1280       1290       1300       1310       1320
CGCCGGAGGGCCAAGCGTAGCCCTAAGCATCACTCACAGCGGGCCAGGAAGAAGAATAAG
 R  R  R  A::K  R  S  P  K  H  H  S  Q  R  A  R  K  K  N  K
     1330       1340       1350       1360       1370       1380
AACTGCCGGCGCCACTCGCTCTATGTGGACTTCAGCGATGTGGGCTGGAATGACTGGATT
 N  C  R  R  H  S  L  Y  V  D  F  S  D  V  G  W  N  D  W  I
     1390       1400       1410       1420       1430       1440
GTGGCCCCACCAGGCTACCAGGCCTTCTACTGCCATGGGGACTGCCCCTTTCCACTGGCT
 V  A  P  P  G  Y  Q  A  F  Y  C  H  G  D  C  P  F  P  L  A
     1450       1460       1470       1480       1490       1500
GACCACCTCAACTCAACCAACCATGCCATTGTGCAGACCCTGGTCAATTCTGTCAATTCC
 D  H  L  N  S  T  N  H  A  I  V  Q  T  L  V  N  S  V  N  S
     1510       1520       1530       1540       1550       1560
AGTATCCCCAAAGCCTGTTGTGTGCCCACTGAACTGAGTGCCATCTCCATGCTGTACCTG
 S  I  P  K  A  C  C  V  P  T  E  L  S  A  I  S  M  L  Y  L
     1570       1580       1590       1600       1610       1620
GATGAGTATGATAAGGTGGTACTGAAAAATTATCAGGAGATGGTAGTAGAGGGATGTGGG
 D  E  Y  D  K  V  V  L  K  N  Y  Q  E  M  V  V  E  G  C  G
     1630       1640       1650       1660       1670       1680
TGCCGCTGAGATCAGGCAGTCCTTGAGGATAGACAGATATACACACACACACACACACAC
 C  R  *
     1690       1700       1710       1720       1730       1740
CACATACACCACACACACACGTTCCCATCCACTCACCCACACACTACACAGACTGCTTCC
     1750       1760       1770       1780       1790       1800
TTATAGATGGACTTTTATTTAAAAAAAAAAAAAAAAAAAAATGGAAAAAATCCCTAAACATT
     1810       1820       1830       1840       1850       1860
CACCTTGACCTTATTTATGACTTTACGTGCAAATGTTTTGACCATATTGATCATATATTT
     1870       1880       1890       1900       1910       1920
TGACAAAATATATTTATAACTACGTATTAAAAGAAAAAAATAAAATGAGTCATTATTTTA
     1930
AAAAAAAAAAAAAAA
```

FIG. 3-2